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DT Rec'd PCT/PTO 18 JAN 2005

APPENDIX A
INTERNATIONAL SEARCH REPORT
PCT/US2003/022584

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 0492479-0030	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, Item 5 below.	
International application No. PCT/US 03/ 22584	International filing date (day/month/year) 18/07/2003	(Earliest) Priority Date (day/month/year) 19/07/2002
Applicant THE GENERAL HOSPITAL CORPORATION		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 9 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 03/22584

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/4015 A61P37/04 A61K47/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 612 037 A (HUEBNER ROBERT C ET AL) 18 March 1997 (1997-03-18)	1,5-7, 13,14, 19, 23-26, 28,32, 33,41, 51,52, 56,57
Y	column 1, line 49 -column 2, line 25 column 3, line 15-58; claims 1,4-6; examples 2-4 --- -/--	1-62

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

4 December 2003

Date of mailing of the international search report

19/12/2003

Name and mailing address of the ISA

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Greif, G

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/22584

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SHARMA S K ET AL: "Maleimide-assisted on-resin macrocyclization" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 37, no. 32, 5 August 1996 (1996-08-05), pages 5665-5668, XP004030506 ISSN: 0040-4039 the whole document	23-26
X	HOLTSBERG F W ET AL: "Poly(ethylene glycol) (PEG) conjugated arginine deiminase: effects of PEG formulations on its pharmacological properties" JOURNAL OF CONTROLLED RELEASE, ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, NL, vol. 80, no. 1-3, 23 April 2002 (2002-04-23), pages 259-271, XP004348640 ISSN: 0168-3659 abstract	1,10,14, 19,32, 33,40,41
Y	page 263, right-hand column, paragraph 2; figure 1	1-30
X	LIU X ET AL: "Strategies for the synthesis of fluorescently labelled PNA" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 41, no. 32, 5 August 2000 (2000-08-05), pages 6153-6156, XP004243532 ISSN: 0040-4039	1,7,14, 15, 17-20, 23,32,41
Y	the whole document	32-40
X	BIENIARZ C ET AL: "EXTENDED LENGTH HETEROBIFUNCTIONAL COUPLING AGENTS FOR PROTEIN CONJUGATIONS" BIOCONJUGATE CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, no. 7, 1996, pages 88-95, XP000946835 ISSN: 1043-1802	1-3,5,6, 13,14, 23-25, 28,32,33
Y	the whole document	1-59
X	PIERCE : "NHS-Esters-Maleimide Crosslinkers" WWW.PIERCENET.COM, 'Online! 27 June 2002 (2002-06-27), XP002263722 Retrieved from the Internet: <URL:www.piercenet.com/files/0438sm4.pdf> 'retrieved on 2003-12-02! cited in the application	23-26
Y	the whole document	32-40

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 03/22584

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 605 791 A (ASHKENAZI AVI J ET AL) 25 February 1997 (1997-02-25)	1-3,6-8, 13-20, 32,41, 60-62
Y	abstract column 3, line 29-50 column 5, line 24 -column 6, line 50 column 7, line 18 -column 9, line 14 claims 1-9; example 1	1-59
X	US 5 945 293 A (BURSHTEYN ALEXANDER ET AL) 31 August 1999 (1999-08-31)	1-6, 13-15,33
Y	column 7, line 21-34 column 9, line 25 -column 10, line 60	32-40
X	US 5 591 710 A (HSIA JEN C) 7 January 1997 (1997-01-07)	1-3,5-7, 13,14, 16,22
	column 17, line 5 -column 18, line 10 column 22, line 31 -column 23, line 47	
X	WO 94 02068 A (GEN HOSPITAL CORP) 3 February 1994 (1994-02-03)	1,2, 7-10, 13-21, 23,41, 51-53, 56,57, 60-62
	claims 1-61	
Y	HERRMANN A ET AL: "Peptide-functionalized polyphenylene dendrimers" TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 59, no. 22, 26 May 2003 (2003-05-26), pages 3925-3935, XP004426763 ISSN: 0040-4020 the whole document	32-40
Y	US 5 780 243 A (THACKER JAMES D) 14 July 1998 (1998-07-14) the whole document	1-62
Y	US 5 342 770 A (YAMASAKI NOBUYUKI) 30 August 1994 (1994-08-30) the whole document	1-30
P,X	US 6 514 500 B1 (L ARCHEVEQUE BENOIT ET AL) 4 February 2003 (2003-02-04) column 8, line 36 -column 15, line 25; examples 4,5,9-11,14,15	1-3,6, 13,14
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/22584

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 02 067995 A (RUSSELL-JONES GREGORY JOHN ;RAO KOLLIPARA KOTESHAWA (IN); CHALASAN) 6 September 2002 (2002-09-06) claims 1-105; figure 1	1-3, 5-20,32, 41, 51-53, 56,57
P,X	WO 02 087498 A (UNIV TEXAS) 7 November 2002 (2002-11-07) the whole document	1-3, 5-10, 13-21, 32,41-57
P,X	US 2002/172689 A1 (SCOTT MARK D) 21 November 2002 (2002-11-21) claims 1-69	1-3,5-8, 10-14, 32,41, 51-53, 56,57,59
A	DUBOWCHIK G M ET AL: "Monomethoxytrityl (MMT) as a Versatile Amino Protecting Group for Complex Prodrugs of Anticancer Compounds Sensitive to Strong Acids, Bases and Nucleophiles" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 38, no. 30, 28 July 1997 (1997-07-28), pages 5257-5260, XP004083292 ISSN: 0040-4039 the whole document	1-31
A	BOECKLER C ET AL: "Immunogenicity of new heterobifunctional cross-linking reagents used in the conjugation of synthetic peptides to liposomes" JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER SCIENCE PUBLISHERS B.V.,AMSTERDAM, NL, vol. 191, no. 1, 10 May 1996 (1996-05-10), pages 1-10, XP004020848 ISSN: 0022-1759 the whole document	1-62

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1-62 (all partially)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-62 (all partially)

Present claims 1-62 relate to a product (a conjugate) or a method defined by reference to a desirable characteristic or property, namely

- (i) carrier
- (ii) modifier
- (iii) detectable label
- (iv) diagnostic label

As a consequence, present claims 1-62 relate to an extremely large number of possible conjugates and methods. In fact, the claims contain so many options and possible combinations that a lack of clarity and conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible.

The claims cover all possible products or methods falling under the desirable characteristic or property, which also lacks clarity, but the application provides support in the meaning of Art. 5 PCT for only a limited number of such conjugates.

In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the parts of the claimed conjugates which are disclosed in claims 2-4, 7-12, 14,16,18, 21,22,25-27,29-31,36-40, 46,, 47, and 49, as well as the examples in the description.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 03/22584

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5612037	A	18-03-1997	AU 707143 B2	01-07-1999
			AU 3234295 A	22-02-1996
			CA 2194183 A1	08-02-1996
			EP 0810876 A1	10-12-1997
			FI 970277 A	23-01-1997
			IL 114666 A	22-12-1999
			JP 10503494 T	31-03-1998
			NO 970080 A	09-01-1997
			WO 9603145 A1	08-02-1996
			ZA 9505945 A	21-02-1996
US 5605791	A	25-02-1997	US 5329028 A	12-07-1994
			US 6124435 A	26-09-2000
			US 5889155 A	30-03-1999
			US 6582928 B1	24-06-2003
			US 5929211 A	27-07-1999
US 5945293	A	31-08-1999	CN 1276871 T	13-12-2000
			EP 1023602 A1	02-08-2000
			JP 2001520383 T	30-10-2001
			WO 9919731 A1	22-04-1999
US 5591710	A	07-01-1997	AT 163186 T	15-02-1998
			CA 2169178 A1	23-02-1995
			CN 1133050 A ,B	09-10-1996
			CN 1228962 A	22-09-1999
			CN 1229677 A	29-09-1999
			DE 69408539 D1	19-03-1998
			DE 69408539 T2	18-06-1998
			DK 714407 T3	28-09-1998
			EP 0714407 A1	05-06-1996
			EP 0770627 A1	02-05-1997
			ES 2114227 T3	16-05-1998
			GR 3026609 T3	31-07-1998
			HK 1007858 A1	23-04-1999
			JP 9501681 T	18-02-1997
			WO 9505397 A1	23-02-1995
			US 6048967 A	11-04-2000
			US 5767089 A	16-06-1998
			US 5804561 A	08-09-1998
			US 5725839 A	10-03-1998
			US 5817632 A	06-10-1998
			US 5807831 A	15-09-1998
			US 5824781 A	20-10-1998
			US 5741893 A	21-04-1998
			US 6323175 B1	27-11-2001
			US 5840701 A	24-11-1998
			US 5789376 A	04-08-1998
			US 6458758 B1	01-10-2002
			US 2002013263 A1	31-01-2002
			TW 381022 B	01-02-2000
			TW 529949 B	01-05-2003
			US 5811005 A	22-09-1998
WO 9402068	A	03-02-1994	AU 4778893 A	14-02-1994
			EP 0654973 A1	31-05-1995
			JP 7509467 T	19-10-1995
			WO 9402068 A1	03-02-1994

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 03/22584

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9402068	A	US 5582172 A	10-12-1996
US 5780243	A 14-07-1998	US 5968515 A	19-10-1999
US 5342770	A 30-08-1994	JP 2896580 B2	31-05-1999
		JP 3083583 A	09-04-1991
		DE 69020276 D1	27-07-1995
		DE 69020276 T2	26-10-1995
		EP 0418523 A1	27-03-1991
US 6514500	B1 04-02-2003	US 2003108567 A1	12-06-2003
		US 2003108568 A1	12-06-2003
		AT 252601 T	15-11-2003
		AU 754770 B2	21-11-2002
		AU 4855500 A	05-12-2000
		AU 765753 B2	25-09-2003
		AU 5139300 A	05-12-2000
		BR 0010750 A	26-02-2002
		CA 2363712 A1	23-11-2000
		CA 2373680 A1	23-11-2000
		CN 1350548 T	22-05-2002
		DE 60006100 D1	27-11-2003
		EP 1180121 A1	20-02-2002
		EP 1105409 A2	13-06-2001
		JP 2003508350 T	04-03-2003
		JP 2003527312 T	16-09-2003
		NO 20015584 A	03-01-2002
		WO 0069911 A1	23-11-2000
		WO 0069900 A2	23-11-2000
		US 6329336 B1	11-12-2001
		US 2002049153 A1	25-04-2002
WO 02067995	A 06-09-2002	US 2002192235 A1	19-12-2002
		WO 02067995 A1	06-09-2002
		EP 1363672 A1	26-11-2003
		GB 2374010 A	09-10-2002
WO 02087498	A 07-11-2002	WO 02087498 A2	07-11-2002
		WO 02087497 A2	07-11-2002
		US 2003003048 A1	02-01-2003
		US 2002197261 A1	26-12-2002
US 2002172689	A1 21-11-2002	NONE	